

CLAIM AMENDMENTS

1. (Currently amended) A method for reducing cell aggregation during
~~[Process for the culturing of cells by]~~ continuous perfusion culturing of a cell culture
comprising cell culture medium and animal cells, wherein cell culture medium is added
to the cell culture, the cell culture is circulated over a filter module comprising hollow
fibers in an alternating tangential flow resulting in an outflow of liquid having a lower
animal cell density than the cell culture~~[- and the flow within the filter module is an~~
~~alternating tangential flow]~~, wherein no more than 5% of the animal cells in the culture
form aggregates of at least 5 cells during the continuous perfusion culturing, and
wherein the culturing is continued until animal cells are present in the cell culture at a
density of at least 80×10^6 animal cells/ml.

2. (Currently amended) The method of ~~[Process according to]~~ claim 1,
wherein the cell culture medium is added at a perfusion rate calculated according to
Formula 1:

Perfusion rate=Specific perfusion rate (SPR)*total cell culture volume*viable cell
density

wherein the perfusion rate is expressed in liters per day, ~~[wherein the SPR is the~~
~~specific perfusion rate, i.e. the rate in which the cell culture medium is fed to the cell~~
~~culture expressed as the volume of medium added per viable cell per time unit]~~ and
wherein the viable cell density is the number of viable cells per unit of volume.

3. (Currently amended) The method of ~~[Process according to]~~ claim 2, wherein the
SPR is between 0.01 and 0.3 nL/animal cell/day.

4. (Currently amended) The method of ~~[Process according to]~~ claim 1,
wherein biomass is removed at least once from the cell culture and additional cell culture
medium is added to the cell culture.

5. (Currently amended) The method of ~~[Process according to]~~ claim 4,
wherein the biomass removal is started just before or just after the cells have reached a
steady state.

6. (Currently amended) The method of ~~[Process according to]~~ claim 4, wherein a volume of biomass is removed of between 2 and 40% of the total volume of the cell culture per day.
7. (Currently amended) The method of ~~[Process according to]~~ claim 1, wherein the alternating tangential flow is achieved using one pump to circulate the cell culture within ~~over a~~ the filter module comprising hollow fibers and using another pump to remove the liquid having a lower cell density than the cell culture prior to the filter separation.
8. (Currently amended) The method of ~~[Process according to]~~ claim 1, wherein the animal cells are cultured to a ~~{viable cell density of at least 80×10^6 cells per ml and a}~~ cell viability of at least 90%.
9. (Currently amended) The method of ~~[Process according to]~~ claim 1, wherein no more than 4% of the animal cells in the culture form aggregates of at least 5 cells during the continuous perfusion culturing ~~[the aggregates of at least 5 cells comprise at the most 5% of the total amount of cells].~~
10. (Canceled)
11. (Currently amended) The method of ~~[Process according to]~~ claim 10, wherein the cells are mammalian cells.
12. (Currently amended) The method of ~~[Process according to]~~ claim 11, wherein the mammalian cells are human ~~[PER.C6@]~~ cells.
13. (Currently amended) The method of ~~[Process according to]~~ claim 1, wherein the cells produce a biological substance.
14. (Currently amended) The method of ~~[Process according to]~~ claim 13, wherein the biological substance is a ~~[therapeutic or diagnostic] protein [,-such as a monoclonal antibody, a growth factor or a peptide hormone, an enzyme,] or a polynucleotide [,-such as a viral vector used in gene therapy, or a vaccine, preferably a monoclonal antibody].~~

15. (Currently amended) The method of ~~[Process according to]~~ claim 13, wherein the biological substance is further purified in downstream processing.